Questions for Panel Discussion

March 27, 2014 meeting of the
Molecular and Clinical Genetics Panel

P130017
Cologuard™
Exact Sciences Corporation

1. The Deep-C study met the primary objectives with respect to both required sensitivity and specificity of *Cologuard* compared to colonoscopy, with 92.3% sensitivity for CRC and 86.6% AN specificity.

   With respect to the secondary objectives, *Cologuard* sensitivity is higher than FIT for both CRC and AA (92.3 vs. 73.8 and 42.4 vs. 23.8, respectively). Although not a secondary objective, *Cologuard* AN specificity is lower than FIT (86.6 vs. 94.9).

   a. Do these conclusions adequately demonstrate effectiveness of *Cologuard* within the contexts of the proposed intended use and current recommendations for CRC screening?

   b. Based on the results of the pivotal clinical study, do the data provided allow for adequate assessment of the benefits and risks of *Cologuard*?

2. Are there patient subgroups, such as age (e.g., ages 75-79, 80-84, 85 and above), gender, and race/ethnicity where considerations for device performance merit additional labeling?

3. The Deep-C study conducted by Exact Sciences was not designed to provide follow-up data on patients that tested negative with *Cologuard*.

   a. What is appropriate labeling to assure safety and effectiveness for follow-up evaluation of patients testing negative with *Cologuard?* The FDA would like feedback on follow-up test interval and modality, use of guidelines, and other possible follow-up approaches.

4. The proposed device claim does not rule out repeating testing as part of a colorectal cancer screening program. Cross-sectional performance at one time point may not translate to longitudinal performance over time. Data was not provided to support repeat testing with *Cologuard*.

   a. *Cologuard* claims do not specify a testing interval. Please discuss whether a longitudinal study should be required to address long-term safety and effectiveness.

5. Assuming that a longitudinal study is needed to evaluate performance with *Cologuard*, please comment on the following:

a. Is comparison to a recommended CRC screening option (e.g., annual FIT) needed to evaluate study results and to mitigate study limitations as currently proposed by the sponsor (such as controlling for incident CRC cases, lack of objective criteria for evaluating study results)?

b. Is the proposed post-approval study adequate to address the following issues?

    i. Performance (e.g., number of test negative to positive conversions, diagnostic yield of significant findings, predictive values, adherence to screening and diagnostic follow-up);

    ii. Performance across different clinicopathologic characteristics;

    iii. Safety concerns (e.g., in the sponsor's proposal, subjects would forgo annual FIT screening during the study duration and repeat *Cologuard* testing will occur after 3 years).

c. Are there any additional considerations that should be taken into account for the post-approval study?